THE VALUE OF SINGLE DOSE FLUCLOXACILLIN IN CLEAN MAJOR SURGICAL OPERATIONS

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DECLARATION

I declare that this dissertation is my original work and has not been presented for a degree in any other university.

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DEDICATION

To my wife Eunice and daughter Kimberly for always being there for me and for the encouragement.

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SUMMARY

A Randomized Prospective study to review the value of single dose Flucloxacillin as antibiotic prophylaxis in clean major surgical operations (Thyroidectomy, herniorrhaphy and mastectomy) was carried out at Kenyatta National Hospital, general surgical unit.

Patients were recruited according to Inclusion/Exclusion criteria and randomized into two groups. One to receive the antibiotic and the other group not receiving antibiotic prophylaxis.

The study used flucloxacillin as antibiotic prophylaxis with randomization of patients receiving the antibiotic at induction of anaesthesia, as a single bolus dose intravenously.

The surgical outcome was gauged by the rate of surgical wound infection in the wards and within 14 days post operatively.

The data was analysed after compilation of the questionnaires.

The age range was 17 years to 62 years with a mean age of 32 years.

380 patients were recruited to the study;

Female to Male ratio was 2:1 with 256 females and 124 males.

133 (35%) patients underwent mastectomy, 125 (33%) Thyroidectomy and 122 (32%) Herniorrhaphy.

188 received antibiotic prophylaxis and 1 (0.5%) out of this group developed wound infection.

192 patients did not receive prophylaxis and 3 (1.6%) out of this group developed wound infection.
Thus fewer patients developed wound infection with antibiotic prophylaxis compared to those who did not receive any prophylaxis.

These data can be used as a baseline to develop guidelines and standing orders for surgical prophylactic regimens.

INTRODUCTION

Surgical wound infection is a major cause of morbidity and mortality. By prolonging hospital stay, it also increases cost of care.

Antibiotic prophylaxis is well established in clean-contaminated surgical operations, based on several prospective randomized trials and meta-analysis (1) The use of antibiotic prophylaxis in clean surgery especially implant surgery is also well established. Benefit of antibiotic prophylaxis is also being seen in some groups of patients undergoing clean surgery e.g. Breast Surgery.

Dose schedules for antibiotic prophylaxis have also been studied with several large scale studies showing benefit of single dose prophylaxis compared to multiple dosing (2,3,4,5). This is given at induction of anaesthesia by the anaesthetist.

Surgical site infection for a skin wound at any site is usually due to Staphylococcus aureus, and 90% remain susceptible to Flucloxacillin (6).

In this study, the value of single dose Flucloxacillin in clean major surgical operations namely thyroidectomy, herniorrhaphy and mastectomy was evaluated. The surgical out come was gauged by wound infection rate.

LITERATURE REVIEW

Historical perspective

About 150 years ago Pasteur and Koch described the infective properties of bacteria. Acting on this information, Lister and Semmelweis demonstrated that measures designed to reduce the number of bacteria reaching a wound could also reduce the number of invasive and lethal infections. Up to that time infection had followed most surgical procedures, so that these scientists and others, in developing the principles of antisepsis and asepsis, were opening a new era in surgical practice. Antibiotics became generally available about 60 years ago and received an over enthusiastic welcome, wounds were dusted and irrigated with antibiotics, patients of all kinds were given antibiotics with all sorts of operations. Undoubtedly, a few patients benefited, but probably just as many suffered. Toxic reactions were common and hospitals became breeding grounds for antibiotic resistant organisms. It gradually became clear that aseptic precautions and thoughtful, gentle surgical techniques were as important as ever.

Experience also showed that antibiotics could help only a particular group of patients and then only during a short, critical period in their management.

Miles and Burke laid the scientific basis for the use of prophylactic antibiotics in surgery in the late 1950's (7), when they were able to show that infections could be prevented only when antimicrobial were given prior to or at the time of the infectious challenge. Antibiotics given 3 hours following the challenge with infectious bacteria were ineffective in preventing infection.

A surgical incision exposes normally sterile tissues to a non-sterile environment; some contamination occurs with any operation. Bacteria may start multiplying before effective host defenses are established, and if initially present in a concentration exceeding 100,000-organisms/gram tissue, may exceed the host defense capacity.

There is a point at which the infecting micro-organisms must make their initial lodgement in the tissue. It's elimination or its persistence as a staging area for further invasion depends largely on the state of the antibacterial defenses of the tissue surrounding this landing site.

Early inflammation is a critical period marked by a number of physiologic and biochemical reactions to the contamination. This time has been called the "decisive period in the defense against bacterial invasion"(8).

In their normal state, tissue defenses appear to be most efficient over a very short period of time, usually within the first three hours of tissue contamination.
If they become inoperative before the contaminating organisms are killed, the bacteria multiply and produce an increased area of tissue damage. An understanding of the events occurring in this decisive period is most important in determining the means by which host defenses can be bolstered by exogenous substances such as antibiotics. The crucial nature of this decisive period was underlined by the experimental finding that maximum inhibition of the tissue defenses immediately before, or simultaneously with, initial contamination resulted in the greatest lesion size.

These results suggest that there may be particular value in enhancing most defenses during the critical period. Antibiotic substances therefore augment the natural resistance in the invaded tissue. There is a short effective period during which it is possible to augment the host's antibacterial mechanisms with an antibiotic.

Studies have shown that if penicillin is given at the same time the wound is contaminated, the resulting lesion will be similar to one produced by an auto claved (i.e. killed) bacterial suspension.

If on the other hand, tissue is contaminated and penicillin is not administered until three hours after the invasion, the lesion will be similar to the one seen in an infected animal given no penicillin at all (9).

This has been shown to be a general effect of antibiotics and not peculiar to penicillin. (10) Following closure of the wound, its environment is sealed by local intravascular coagulation and the events of early inflammation which initiate wound healing. This may explain why post-operative administration of antibiotics is ineffective in preventing wound infection. Antibiotics administered pre-operatively diffuse into the peripheral compartment, in this case the wound fluid. Since the wound is saturated with antimicrobial at the time it becomes contaminated, potentially invading bacteria are inhibited from multiplying and many are killed. Controlled trial demonstrating the efficacy of antibiotic prophylaxis in potentially contaminated operations was reported by Bernard and Cole (1).

Strachan and Colleagues performed the prospective controlled trial, which investigated the proper pre-operative duration of antibiotic prophylaxis in 1977, in patients undergoing cholecystectomy.

Single preoperative dose of cefazolin was compared with a regimen of cefazolin given for a period of 5 days after operation.

The infection rate following a single dose of antibiotics was 3%. That following multiple post-operative dosing was 5% (11). Clarke et. al. similarly studied single dose versus multiple dose prophylaxis for colonic surgery in a prospective randomized trial of 1003 patients, wound infection rate for single dose prophylaxis was 4.3% compared to 6.9% in multiple dosing prophylaxis (12).

A meta analysis compared two dose schedules of cefotaxime in a prospective randomized 226 centre study of 3,670 patients undergoing abdominal, gynaecologic and urologic surgery. Schedule A consisted of a single pre-operative dose and schedule B consisted of one pre operative dose followed by two post-operative doses. There was no significant difference in the frequency of wound infection between the two schedules. Schedule B was associated with a significantly higher incidence of post-operative pyrexia, further antibiotic therapy, local side effects and extended hospital stay (13).

Similar studies have shown benefit of single dose prophylaxis compared to multiple dosing.

Today antibiotic prophylaxis is an established practice and the principles for optimal preventive antibiotic administration are widely accepted.

Risk of Infection

The risk of developing a wound infection has traditionally been determined by stratifying operations into classes: - clean, clean-contaminated, contaminated and dirty, based on the relative degree of intra-operative bacterial contamination (14). Other important factors such as the functional state of host defenses e.g. shock, immuno-deficient state or old age, amount of tissue trauma engendered by the operation and long duration of operation (the critical time is procedure - specific), also determine the risk of developing a wound infection.

The presence of co-morbidities at the time of surgery increase, risk of wound infection. The American Society of Anesthesiologists (ASA) has devised a preoperative risk score based on physical status (15).

Any patient exhibiting one or more of these risk factors should be given antibiotic prophylaxis.

In addition prophylaxis should be administered whenever a prosthesis is to be inserted during the operation or for patients on treatment with steroids, anti-neoplastic agents, immunosuppressive therapy and radiotherapy (16,17).

The most common organisms in simple wound infection are gram positive cocci and mainly staphylococcus aureus, these organisms predominate in the infectious complications following clean surgical procedures (18).

Grading the severity of wound infections to assess the efficacy of prophylaxis uses clinical assessment with the scheme modified from Hulton et al (1985) classifying four grades.

Grade	**Clinical Assessment**
1	Erythema around wound margins greater than would be expected after 24 hours. No wound ooze.
2	Erythematous wound with serous serosanguinous discharge or pustules close to wound. Patient usually apyrexial.
3	Purulent discharge from part of wound without separation of the edges. Patient may be pyrexial.
4	Purulent, often blood stained discharge, for most of incision with separation of wound dehiscence. Patient usually pyrexial

It is also important to understand the pharmaco dynamics of the antibiotics used, so that the correct timing of doses is followed. Studies have shown that the infection rate increases as the concentration of antibiotics decreases during surgery (19,20,21).

In addition to the general kinetics of the drugs, the body's kinetics must be considered such as the effects of organ failure. Renal and hepatic dysfunction reduces the body's metabolism and clearance of antibiotics. A reduction in the frequency of dosing is therefore required (22,23).

The principles of antibiotic prophylaxis are:

1) Use an antibiotic with efficacy against the bacteria likely to contaminate the wound as demonstrated in a controlled clinical trial.

2) Use full doses of the chosen antibiotic.

3) Administer the antibiotics pre-operatively at a time such that effective tissue concentration will have been achieved when intraoperative contamination occurs.

4) If the operation is prolonged beyond 3 or 4 hours or blood loss of over 1500ml give another dose. Otherwise single dose prophylaxis is effective in most clinical situations (24,25,26).

5) Employ antibiotic prophylaxis whenever the risk of wound infection is increased.

Antibiotic prophylaxis is well established for clean - contaminated and contaminated surgical cases. New indications for use in clean elective procedures such as mastectomy and herniorrhaphy are being supported recently on the basis of large studies on the pharmaco-economics of infections (27).

Antibiotic prophylaxis has become standard care not only in operation characterized by high infection rates but also in the vast majority of clean surgical procedures, including those that use foreign materials, graft or prosthetic devices as well as implant surgery (28,29).

Abo Rahmy evaluated antibiotic prophylaxis using cetriaxone in 1,524 patients undergoing hernia repair and observed surgical wound infection rate of 0.06%. This was much lower than when no prophylaxis was used (30).

Some groups of patients undergoing clean surgery benefit from the provision of antibiotic prophylaxis against wound infection. Breast surgery may belong to this category because several substantial, studies have reported that it is accompanied by an unacceptably high rate of wound infection. However, only two clinical trials have addressed this issue and both produced equivocal results. Resolution of this problem is important because, aside from the usual advantages obtained by preventing such complications, wound infection diminishes the proportion of patients with breast cancer who start adjuvant regimes within an optimum time after surgery (31).

The true rates of septic complications in patients undergoing clean surgery are grossly under reported with up to 72% of all complications occurring, undetected by the surgical team, after discharge from hospital.

The implied costs of these infections, coupled with the costs to both the patient and the community services, suggest that antibiotic prophylaxis should be seriously considered for many types of clean surgery (32).

Similarly single dose antibiotic prophylaxis was found beneficial in reducing rate of wound infection after umbilical and incisional hernia repair (33,34).

Cefuroxime was also evaluated as antibiotic prophylaxis and was associated with a low incidence of post operative would infection in patients undergoing clean neurosurgery (35).

Flucloxacillin as antibiotic prophylaxis has been used frequently in surgical procedures where staphylococcus aureus is the main pathogen; Steer et al evaluated flucloxacillin against teicoplanin and found no significant difference in the bactericidal rates of the two antibiotics (36).

The effectiveness of antibiotic prophylaxis in preventing deep and superficial wound infections in herniorrhaphy and mastectomy, especially if prophylaxis is directed against staphylococcus aureus, was evaluated by Hopkins et al. and showed results of decrease of upto 50% in wound infections (37).

Surgical site infection for a skin wound at any site is usually due to staphylococcus aureus, and 90% remain susceptible to flucloxacillin.

Mounsey J.P et. al. in a prospective randomized trial for patients undergoing pacemaker implantation used single dose flucloxacillin to determine whether antibiotic prophylaxis was efficacious. Over a 17-month period, 473 patients were recruited. Flucloxacillin significantly reduced the incidence of infective complications. The study recommended routine use of antibiotic prophylaxis (38).

Flucloxacillin was also evaluated as antibiotic prophylaxis in hernia operations at Rockingham/Kwinana Hospital in Australia in 1999 (39), and in skin surgery at Papworth Hospital in United Kingdom (40), both studies showed significant reduction in wound infection.

Abele-Horn and others in their study used flucloxacillin to successfully treat persistent wound infection due to Staphylococcus aureus following herniotomy and mesh repair of inguinal hernia (41).

Flucloxacillin has therefore been recommended for use as antibiotic prophylaxis in surgery where surgical site infection is predominantly Staphylococcus aureus and has been incorporated in many antibiotic guidelines for this use (42, 43).

RATIONALE OF THE STUDY

Antibiotic prophylaxis is used routinely at Kenyatta National Hospital for most clean-contaminated and contaminated surgical cases. However, antibiotics prescribed are often continued beyond the duration of prophylaxis. No study on antibiotic prophylaxis and surgical outcome has been carried out at Kenyatta National Hospital. This study looks at single dose prophylaxis in clean surgical cases and aims at highlighting the rational use of antibiotic prophylaxis in order to improve quality of patient care, reduce cost as well as limit emergence of resistant bacterial strains.

BROAD OBJECTIVES

To determine the rate of surgical wound infection in clean surgical operation at Kenyatta National Hospital by using flucloxacillin as antibiotic prophylaxis in a randomised prospective study.

SPECIFIC OBJECTIVES

1) To determine the rate of surgical wound infection in thyroidectomy, herniorrhaphy and mastectomy at Kenyatta National Hospital using single dose flucloxacillin.

2) To determine rate of surgical wound infection in thyroidectomy, herniorrhaphy and mastectomy at Kenyatta National Hospital without use of antibiotic prophylaxis.

3) To highlight the rational use of antibiotic prophylaxis.

MATERIALS AND METHODS

STUDY DESIGN

A randomized prospective descriptive study of patients undergoing clean surgical operations was done. Patients were recruited according to the inclusion, exclusions criteria during admissions.

The patients were randomized for administration of single dose Flucloxacillin 1g intravenously at induction of anaethesia. Both groups were followed up in the wards and wounds monitored until discharge.

The patients were seen in the surgical outpatient clinic on the fourteenth post operative day and the wounds inspected for wound infections. The findings were entered into a questionnaire and analysed.

STUDY POPULATION/SUBJECTS

Patients aged 13 years and above and below 65 years of both sexes prepared for elective clean surgical operations including thyroidectomy, herniorrhaphy and mastectomy.

STUDY SITE/AREA

The study was conducted at Kenyatta National Hospital general surgical unit. This included the three general surgical wards 5A, 5B, 5D; the operating theaters, the surgical outpatient clinic and the records department.

INCLUSION CRITERIA

1) Patients both male and female above 13 years and below 65 years.

2) Patients admitted for the following elective clean surgical operations.

   - Thyroidectomy
   - Herniorrhaphy
   - Mastectomy

3) Patients giving an informed written consent to be included in the study. Consent was also be obtained from next of kin where applicable.

EXCLUSION CRITERIA

1) Patients below 13 years or above 65 years of age.
2) Patients who did not give consent.
3) Patients not fit for surgery.
4) Patients with above diagnosis not operated on.
5) Patients who were already on some antibiotics
6) Patients with history of sensitivity to penicillins
7) Patients known to be HIV positive

PATIENT RECRUITMENT

Patients were recruited at admission into the wards according to the inclusion/exclusion criteria. In the operating theaters administration of antibiotic prophylaxis to the patients was done on a randomized basis at induction of anaesthesia. The table of random numbers was used for the randomization process.

Patients were followed up in the wards for wound inspection and thereafter by the fourteenth post-operative day. The data was entered into the questionnaire.

STATISTICAL ANALYSIS

Chi-Square was used to calculate statistical significance at 95% confidence interval. Analysis by the SPSS PC analysis package version 10 was done.

Numbers needed to treat (NNT) was calculated:

$$\text{NNT} = \frac{\textbf{1-(Expected baseline risk x (1-odds ratio)}}{\textbf{(1-Expected baseline risk) x expected baseline risk x (1-odds ratio)}}$$

DATA COLLECTION

This was done in the form of a pretested questionnaire designed by the author and completed by the same on reviewing the patients in the wards and surgical out patient clinic on day 14 post operatively.

The questionnaire had various sections.

1) Filing section, which included study number
2) Demographic characteristics
3) Operative procedure
4) Antibiotic prophylaxis
5) Outcome

PRE-TESTING

Before the study, 20 questionnaires were filled to test its formulations and willingness of patients to participate in the study. Corrections were made on the questionnaire accordingly.

PATIENTS AND METHODS

The study was carried out at the Kenyatta National Hospital General Surgical Unit. Patients recruited for the study, were those admitted for elective clean surgical operations, as per the inclusion/exclusion criteria,

an informed written consent was obtained. Antibiotic prophylaxis (1g Flucloxacillin intravenously) administered on a randomized basis at induction of anaesthesia was recorded and those patients not receiving prophylaxis were also noted down. Follow up of the patients in the ward for wound inspection was done before discharge and on the forteenth post-operative day at the surgical outpatient clinic.

Analysis of the data collected was done using Chi-Square at 95% confidence level.

DATA COLLECTION, MANAGEMENT AND ANALYSIS

Various variables collected in the questionnaires were be used to complete the data sheet. This was entered into computer and analysed by the SPSS PC analysis package version 10.

ETHICS AND CONFIDENTIALITY

The research protocol was submitted to the Kenyatta National Hospital Ethical and Research Committee for approval before embarking on the study.

Patients included in the study gave informed written consent. All data collected was handled confidentially. Patients identifying charts were kept confidential at all times.

RESULTS

Data on 380 patients who underwent thyroidectomy, herniorrhaphy and mastectomy and either received or did not receive Flucloxacillin antibiotic prophylaxis between May 2002 and October 2002 at Kenyatta National Hospital was analysed.

The age range was 17 years to 62 years with a mean age of 32 years.

Male: Female Ratio

The patients were predominantly females who numbered 256(67%) while males were 124 (33%) in a ratio of 2:1. (Fig 1) and (Table 1)

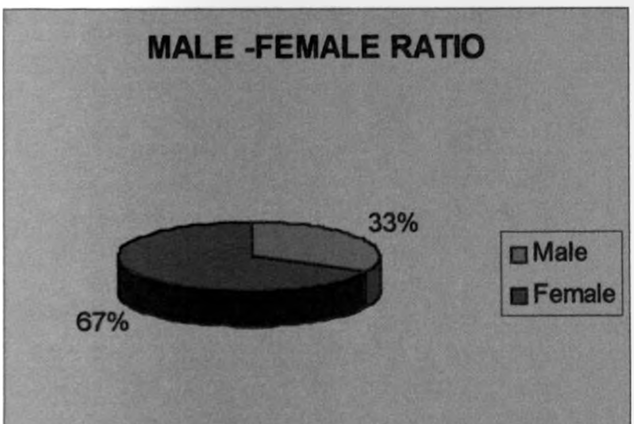

FIGURE 1

TABLE 1

	No. of Patients	Percent
Male	124	33
Female	256	67
Total	380	100

Age Category

The 380 patients were distributed in six age categories.

The most predominant age category was 41 to 50 with 114 (30%) patients, followed closely by 31 to 40 with 111 (29.2%) patients 61 and above age category had only 7 (1.8%) patients while 10 to 20 category had 12 (3.2%) patients. (Table 2).

TABLE 2

	No. of Patients	Percent
10 to 20	12	3.2
21 to30	85	22.4
31 to 40	111	29.2
41 to 50	114	30.0
51 to 60	51	13.4
61 and above	7	1.8
Total	380	100.0

Age category versus sex

The sex according to age category was analysed.

Out of the 124 male patients, the predominant age category was 21 to 30 with 41 (33%) patients, followed by 31 to 40 and 41 to 50 both with 33 (27%) patients each. 10 to 20 category had 9 (7%) patients while 61 and above had none.

Out of the 256 female patients, the predominant age category was 41 to 50 with 81 (32%) patients, followed by 31 to 40 age category with 78 (30%) patients. Age category 21 to 30 had 44 (17%) patients and 51 to 60 had 43 (17%) patients. 61 and above had 7 (3%) patients while 10 to 20 had 3 (1%) patients. (Table 3).

TABLE 3

		sex		Total
age category		Male	Female	
10 to 20	No. of Patients	9	3	12
	Percent	7	1	3
21 to30	No. of Patients	41	44	85
	Percent	33	17	22
31 to 40	No. of Patients	33	78	111
	Percent	27	30	29
41 to 50	No. of Patients	33	81	114
	Percent	27	32	30
51 to 60	No. of Patients	8	43	51
	Percent	6	17	13
61 and above	No. of Patients	0	7	7
	Percent	0	3	2
Total	No. of Patients	124	256	380
	Percent	100	100	100

Age category versus operative procedure

The predominant age category for the Thyroidectomy patients was 21 to 30 and 31 to 40, each with 34% of the patients.
In the Herniorraphy patients, 35% were in the age category of 21 to 30. Age category 31 to 40 and 41 to 50 each had 25% of the patients.
The predominant age category for the mastectomy patients was 41 to 50 with 56% of the patients. (Table 4)

TABLE 4

		Operative procedure			Total
Age category		Thyroidectomy	Herniorrhaphy	Mastectomy	
10 to 20	No. of Patients	4	8	0	12
	Percent	3	7	0	3
21 to30	No. of Patients	42	43	0	85
	Percent	34	35	0	22
31 to 40	No. of Patients	42	31	38	111
	Percent	34	25	29	29
41 to 50	No. of Patients	27	31	56	114
	Percent	22	25	42	30
51 to 60	No. of Patients	9	9	33	51
	Percent	7	7	25	13
61 and above	No. of Patients	1	0	6	7
	Percent	1	0	5	2
Total	No. of Patients	125	122	133	380
	Percent	100	100	100	100

Age category versus Antibiotic prophylaxis

The Antibiotic Prophylaxis according to age category was analysed.

Out of the 188 patients who received antibiotic prophylaxis, the predominant age category was 41 to 50 with 60 (32%) patients.

This was followed by age category 31 to 40 with 49 (26%) patients. 61 and above had only 2 (1%) patients while 10 to 20 had 6 (3%) patients.

Of the 192 patients who did not receive antibiotic prophylaxis, the predominant age category was 31 to 40 with 62 (32%) patients then age category 41 to 50 with 54 (28%) patients. Category 21 to 30 had 42 (22%) patients, while 61 and above had 5 (3%) patients. 10 to 20 category had 6 (3%) patients. (Table 5)

TABLE 5

		Antibiotic prophylaxis		Total
Age category		Given	Not given	
10 to 20	No. of Patients	6	6	12
	Percent	3	3	3
21 to30	No. of Patients	43	42	85
	Percent	23	22	22
31 to 40	No. of Patients	49	62	111
	Percent	26	32	29
41 to 50	No. of Patients	60	54	114
	Percent	32	28	30
51 to 60	No. of Patients	28	23	51
	Percent	15	12	13
61 and above	No. of Patients	2	5	7
	Percent	1	3	2
Total	No. of Patients	188	192	380
	Percent	100	100	100

Sex versus Operative Procedure

Out of the 125 patients who underwent thyroidectomy, 95% were females and males constituted only 5%. In contrast 95% of the 122 patients who underwent herniorrhaphy were males with females being 5%.

Out of the 133 mastectomy patients 98% were females and only 2% were males. (Table 6).

TABLE 6

		Operative procedure			Total
Sex		Thyroidectomy	Herniorrhaphy	Mastectomy	
Male	No. of Patients	6	116	2	124
	Percent	5	95	2	33
Female	No. of Patients	119	6	131	256
	Percent	95	5	98	67
Total	No. of Patients	125	122	133	380
	Percent	100	100	100	100

Antibiotic prophylaxis

In the study 188 patients (49%) received flucloxacillin as antibiotic prophylaxis while 192 patients (51%) did not receive antibiotic prophylaxis (Table 7).

TABLE 7

	Frequency	Percent
Given	188	49
Not given	192	51
Total	380	100

Operative procedure versus No. of patients

The commonest operative procedure was mastectomy 133 (35%), followed by thyroidectomy 126 (33%) then herniorrhaphy 122 (32%). (Fig 2) and (Table 8)

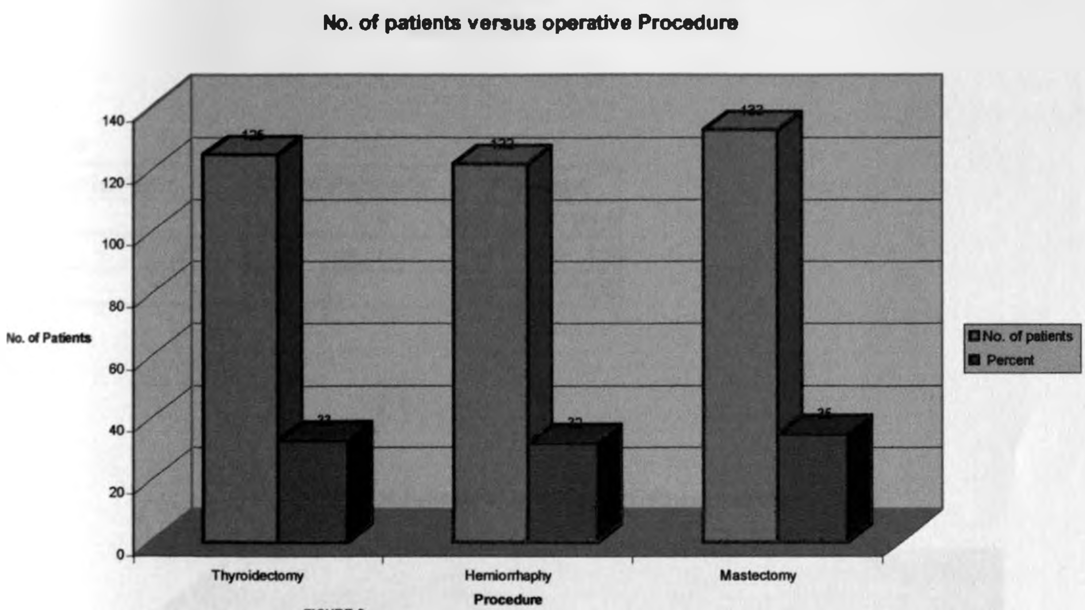

FIGURE 2

TABLE 8

	No. of patients	Percent
Thyroidectomy	125	33
Herniorrhaphy	122	32
Mastectomy	133	35
Total	380	100

Surgical Wound Infection Rate Versus Number of Patients

Out of the 380 patients recruited to the study, 4 (1.1%) developed wound infection, all grade 1. The rest 376 (98.9%) did not develop any wound infection. (Table 9) and (Fig3).

TABLE 9

Wound infection	No. of Patients	Percent
None	376	98.9
Grade 1	4	1.1
Total	380	100

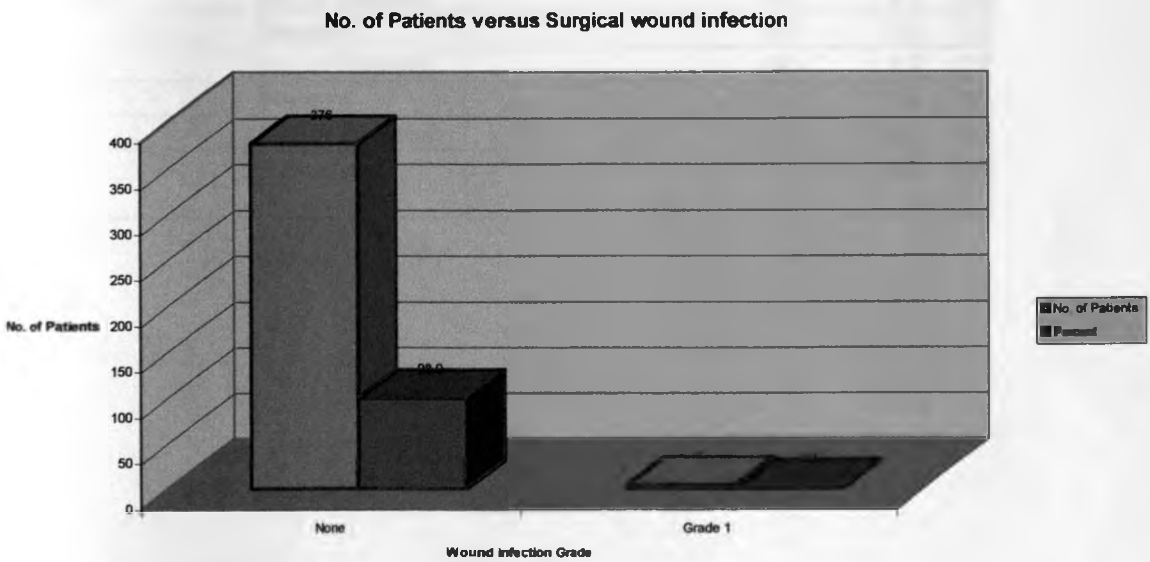

FIGURE 3

Operative procedure versus antibiotic prophylaxis

Of the 188 patients given antibiotic prophylaxis, 32% underwent thyroidectomy, 31% herniorrhaphy and 36% mastectomy.

Of the 192 patients who did not receive prophylaxis 33% underwent thyroidectomy, 33% herniorrhaphy and 34% mastectomy. (Table 10)

TABLE 10

		Antibiotic prophylaxis		Total
Operative procedure		Given	Not given	
Thyroidectomy	No. of Patients	61	64	125
	Percent	32	33	33
Herniorrhaphy	No. of Patients	59	63	122
	Percent	31	33	32
Mastectomy	No. of Patients	68	65	133
	Percent	36	34	35
Total	No. of Patients	188	192	380
	Percent	100	100	100

Operative procedure versus surgical wound infection rate

None of the 125 thyroidectomy patients developed wound infection.

Out of the 122 who underwent herniorrhaphy, 1 developed a grade 1 surgical wound infection.

Out of the 133 mastectomy patients, 3 developed grade 1 surgical wound infection. (Table 11)

TABLE 11

	Surgical wound infection rate		
Operative procedure	NONE	GRADE 1	
Thyroidectomy	125	0	125
Herniorrhaphy	121	1	122
Mastectomy	130	3	133

Chi – square testing

The chi – square method was used to test for statistical significance

Table 11b

121	1
130	3
Chi	0.357

Antibiotic Prophylaxis versus Wound Infection rate

Out of the patients given antibiotic prophylaxis, 0.5% developed grade 1 wound infection.

Of those patients who did not receive antibiotic prophylaxis 1.6% developed grade 1 wound infection. (Table 12)

TABLE 12

Antibiotic Prophylaxis		Wound infection grade	
		None	Grade 1
Given	Percent	99.5	0.5
Not given	Percent	98.4	1.6

Chi-square testing

The chi-square method was used in testing the statistical significance

TABLE 12b

99.5	**0.5**
8.4	**1.6**
Chi	**0.0158**

From the odds ratio and baseline risk of wound infection the numbers needed to treat (NNT) i.e. the number of patients that must receive prophylaxis in order to prevent one wound infection was calculated according to cook and Sackett (53) and was 143.

DISCUSSION

Infection of the incised skin or soft tissues is a common but potentially avoidable complication of any surgical procedure. Some bacterial contamination of a surgical site is inevitable, either from the patient's own bacterial flora or from the environment.

Prophylactic administration of antibiotics inhibits growth of contaminating bacteria, thus reducing the risk of infection (44,45,46).

However, injudicious use of antibiotics increases the prevalence of antibiotic - resistant bacteria (47) and predisposes the patient to infection with organisms such as Clostridium difficile, a cause of antibiotic - associated Colitis (48).

It is important to emphasize that surgical antibiotic prophylaxis is an adjunct to, not a substitute for, good surgical technique. Antibiotic prophylaxis should be regarded as one component of an effective policy for the control of hospital - acquired infection.

The need for guidelines on surgical antibiotic control measures published by the British Society for Antimicrobial Chemotherapy in 1994 found that policies for surgical prophylaxis existed in only 51% of the hospitals surveyed and compliance was monitored in only half of these (49).

Although a wide range of organisms can cause infections in surgical patients, surgical site infection is usually due to a small number of common pathogens. Only these need to be covered by the antibiotic prescribed (50).

In this study, the choice of flucloxacillin was based on its effectiveness against Staphyloccocus aureus which is usually implicated in surgical site infection for a skin wound at any site.

For surgical wounds, 90% of the staphylococcus aureus remain susceptible to flucloxacillin.

The effectiveness of antibiotic prophylaxis in preventing deep and superficial wound infection in herniorrhaphy and mastectomy, especially if prophylaxis is directed against staphylococcus aureus, was evaluated by Hopkins et al and showed results of decrease of up to 50% in wound infections.

In comparison, this study had a reduction of wound infection rate from 1.6% in the group of patients who did not receive prophylaxis to 0.5% in the group which received prophylaxis, thus reflecting similar outcome to Hopkin's Study.

This is also comparable to that of baseline risk of wound infection for clean surgery without prophylaxis of 1%.(51).

The odds ratio of wound infection with antibiotic prophylaxis was calculated at 0.5%/1.6% (0.3125).

Chi was not statistically significant at 0.0158 for 95% confidence interval.

One of the aims of rationalizing surgical antibiotic prophylaxis is to reduce the inappropriate use of antibiotic thus minimizing the consequences of misuse.

Rates of antibiotics resistance are increasing in all hospitals.

The prevalence of antibiotic resistance in any population is related to the proportion of the population that receives antibiotics, and also the total antibiotic exposure (52). Surgical wound infections also increase the length of hospitals stay and antibiotic prophylaxis can reduce this period.

From the odds ratio and baseline risk of wound infection the numbers needed to treat (NNT) i.e. the number of patients that must receive prophylaxis in order to prevent one wound infection was calculated according to cook and Sackett (53) and was 143.

Reduction in overall antibiotic consumption highlights the importance of restricting prophylaxis to a single dose. Every additional prophylactic dose that is administered increases the baseline risk of wound infection that is required for prophylaxis to reduce overall antibiotic consumption. Increasing the number of doses of prophylaxis also adds to the cost.

The final decision regarding the benefits and risks of prophylaxis for an individual patient will depend on:

- The patient's risk of the consequences of surgical site infection
- The potential severity of the consequences of surgical site infection
- The effectiveness of prophylaxis in that operation
- The consequences of prophylaxis for that patient (e.g. increase risk of colitis)

A comprehensive risk assessment should be part of the process of choosing the appropriate antibiotic (54). This should include economic considerations, such as acquisition costs of the drug and costs of administration and preparation, set against consequences of failure of prophylaxis and the possible adverse events.

Prescribers need to be aware that infections that occur in patients who receive prophylaxis are usually caused by bacteria that remain sensitive to the prophylactic regimes. Implementation of prophylaxis should not be accompanied by radical changes in treatment policy because such changes may wipe out the benefits of prophylaxis, and lead to major drug-resistance problems (55).

A past history of a serious adverse drug reaction should preclude administration of a particular antibiotic.

Reactions to penicillin may occur because of allergy to the parent compound or its metabolites.

In patients allergic to penicillin, challenge tests can be used to demonstrate cross-reactions with cephalosporins and carbapenems (56).

Policies on surgical prophylaxis should thus recommend an alternative for patients who have a history of allergy to the drug.

In this study a clear history of allergy to penicillin was obtained and patients with positive history excluded from the study.

The period of risk for surgical site infection begins with the incision. The time taken for an antibiotic to reach an effective concentration in any particular tissue reflects its pharmacokinetic profile and the route of administrations.

Administration of penicillin in this study was carried out at induction of anaesthesia by the anaesthetist.

Single dose prophylaxis has been compared to multiple dose antibiotic prophylaxis in many studies. The administration of additional doses has not been found to confer additional prophylactic benefit.

Prophylaxis needs to be confined therefore to the peri operative period (i.e. administration immediately before or during the procedure.)

However, in prolonged surgery extending beyond 3 to 4 hours, the serum antibiotic concentrations progressively decrease to below the minimum inhibitory concentration.

In this case additional prophylactic doses can be given. Similarly, if there is blood loss over 1500ml, additional prophylactic should be given.

In this study, single dose flucloxacillin was given to all the 188 patients who received antibiotic prophylaxis.

Intravenous administration of antibiotic prophylaxis immediately before or after induction of anaesthesia is the most reliable method for ensuring effective serum antibiotic concentration at the time of surgery. Serum concentration after oral or intramuscular administration are determined in part by the rate of absorption, which varies between individuals.

There is relatively little evidence about the effectiveness of orally or intramuscularly administered antibiotic prophylaxis. A further problem is that often the correct time to administration is difficult to guarantee in practice, because, for example, it occurs outside the theatre environment.

Administration of antibiotic prophylaxis by the intravenous route is the only method that is supported by a substantial body of evidence.

This was the route used to administer flucloxacillin in this study.

Antibiotic prophylaxis has become standard care not only in operation characterized by high infection rates but also in the vast majority of clean surgical procedures, including those that use foreign materials, grafts or prosthetic devices as well as non-implant surgery.

However, a group of patients undergoing clean surgery benefit from the provision of antibiotic prophylaxis against wound infection. The wound infection also diminishes the proportion of patients with breast cancer who start adjuvant regimes within an optimum time after surgery.

Bier et al evaluated single dose antibiotic prophylaxis for breast surgery in 97 patients in an open, randomized study and found it to be efficacious (57).

Ranaboldo et al found that the true rates of septic complications in patients undergoing herniorrhaphy are grossly under reported, with up to 72% of all complications occurring, after discharge from hospital.

Flucloxacillin as antibiotic prophylaxis was evaluated in hernia operations and skin surgery with significant reduction in wound infection.

In this study at Kenyatta National Hospital, patients underwent thyroidectomy, mastectomy and herniorrhaphy; all clean surgical operations.

There was reduction in wound infection rate in the group receiving prophylaxis (0.5%) compared to those who did not receive prophylaxis (1.6%).

Introduction of special forms for ordering peri operative antimicrobial prophylaxis has been shown to reduce inappropriate prescribing from 64% to 21% (58).

Prescribing antibiotic prophylaxis in the single dose section of drug prescription forms is also associated with a lower proportion of inappropriate additional doses (58).

All aspects of antibiotic prophylaxis should be recorded in the case notes and/or the drug prescription chart.

Recommended means of facilitating this include the incorporation of a stamp or adhesive into the case records, including nursing checklist, or into integrated care pathways. As an alternative this information can be hand written in the records and/or the drug chart. If prophylaxis is normally indicated, but not given, then the reasons for this should be clearly recorded in the case records (59).

Core indicators for surgical audit need to be in mind. These are mainly two:

Process Measures:

- Was prophylaxis given for an operation included in local guidelines?
- If prophylaxis was given for an operation not included in local guidelines, was a clinical justification for prophylaxis recorded in the case notes?
- Was the first dose of prophylaxis given within 30 minutes of the start of surgery?
- Was the prescription written in the "once-only" sections of the drug prescription chart?
- Was the duration of prophylaxis greater than 24 hours?

Out come Measures:

- Surgical site infection rate.
- Rate of surgical site infection occurring post operatively in patients who receive inappropriate prophylaxis (as defined in guideline) compared with rate of this infection in patients who receive prophylaxis, expressed as a ratio.
- Rate of clostridium difficile infections occuring post operatively in patients who received inappropriate prophylaxis (as defined in guideline) compared with rate of this infection in patients who received appropriate prophylaxis, expressed as a ratio.

The minimum data set for surgical antibiotic prophylaxis should be:

- Date
- Operation performed
- Justification for prophylaxis (e.g. evidence of high risk of surgical site infection) if prophylaxis is given for an operation that is not one of the indications for routine prophylaxis.
- Time of antibiotic administration.
- Elective or emergency.
- Name, dose, route of antibiotic
- Time of surgical incision
- Number of doses given.
- Classification of operation (clean/clean - contaminated/contaminated).
- Previous adverse reactions to antibiotic?
- Duration of operation.
- Second dose indicate?
- Name of anaesthetist.
- Name of surgeon.
- Designation of surgeon.

CONCLUSION

Out of 380 patients recruited into the study 4 (1.1% of all patients) developed surgical wound infection.

Those who received flucloxacillin antibiotic prophylaxis had a lower wound infection rate of 0.5% compared to those who did not receive prophylaxis (1.6%). The wound infection rate without antibiotic prophylaxis (1.6%) was comparable to that of baseline risk of wound infection for clean surgery (1%). (51)

The odds ratio was 0.3125 while the numbers needed to treat (NNT) was 143.

From the results therefore, 143 patients must receive prophylaxis in order to prevent one wound infection. This therefore means that antibiotic prophylaxis for clean surgery is costly.

The compliance was good as the flucloxacillin antibiotic was given as single bolus intravenous dose at induction of anaesthesia by the anaesthetist.

RECOMMENDATION

- Display of prophylaxis regimens according to type of surgery in table format in the operating room and having the anaesthetist note the complete drug regime on the patient's anaesthetic record.
- Development of guidelines and standing orders for antibiotic prophylaxis. This will improve compliance and also enable prophylactic antibiotic audit measures to be carried out.
- Standardize surgical prophylactic regimens in order to reduce cost and combat the emergence of antibiotic resistance.
- Prophylaxis should be given to patients who are at high risk of surgical site infection and if it is likely to reduce overall antibiotic consumptions and costs.

Appendix 1

QUESTIONNAIRE

RATE OF SURGICAL WOUND INFECTIONS AMONG PATIENTS UNDERGOING CLEAN MAJOR SURGICAL OPERATIONS WITH OR WITHOUT ANTIBIOTIC PROPHYLAXIS USING FLUCLOXACILLIN

A **IDENTIFIERS**

Study Number Code

IP. Number

B **DEMOGRAPHIC CHARACTERISTICS**

	Male	Female
Sex		
Age		

C **OPERATIVE PROCEDURE**

1.	**Thyroidectomy**	
2.	**Herniorrhaphy**	
3.	Mastectomy	

D **ANTIBIOTIC PROPHYLAXIS**
(1g Flucloxacillin)

Given	Not given

E OUTCOME

Wound Infections

None	
Grade 1	
2	
3	
4	

Appendix 2

CONSENT BY PATIENT/NEXT OF KIN FOR INCLUSION INTO STUDY ON FLUCLOXACILLIN AS ANTIBIOTIC PROPHYLAXIS IN CLEAN MAJOR SURGERY

I ....of......................... hereby consent to be

included into study on flucloxacillin as antibiotic prophylaxis in clean major surgery.

Clear explanation has been given to me on randomization to either receive or not

receive the antibiotic Flucloxacillin by **Dr...**

I am aware of possible increase in wound infection rate while not receiving

flucloxacillin.

I am also aware of possibility of adverse drug reaction to flucloxacillin.

Date: ....Signed (Patient).........................

I confirm that I have clearly explained to the patient the above named study

protocol, including the benefits (possibility of decreased wound infection rate on

receiving flucloxacillin) and disadvantages (possibility of increased wound infection

rate without flucloxacillin and possible adverse drug reaction to flucloxacillin).

Date......................Signed (Doctor)................................

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RESEARCH PROPOSAL "THE VALUE OF SINGLE DOSE FLUCLOXACILLIN IN CLEAN MAJOR SURGICAL OPERATIONS" (P117/11/2001)

This is to inform you that the Kenyatta National Hospital Ethical and Research Committee has reviewed and approved the revised version of your above cited research proposal.

On behalf of the Committee I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Thank you.

Yours faithfully,

PROF. A.N. GUANTAI
SECRETARY, KNH-ERC

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